

Correlation Between Delayed Therapy and Controlled Seizures in Patients with Epilepsy At Dr. Soepraoen Army Hospital 2019

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Background: Epilepsy is a progressive brain disorder and is diagnosed after at least two unprovoked epileptic seizures occur. Delay in treatment can lead to more epileptic episodes. The number of epileptic episodes before treatment affects the expansion of the epilepsy focus, which becomes a factor in reducing the brain's sensitivity to treatment. **Objective:** Knowing is there any relationship between delayed therapy of ASM administration and controlled epileptic seizures. **Method:** This research method is analytic observation with retrospective approach. Using a total sampling technique, the sample in this study was 41 samples taken from epilepsy patients who were registered in the medical records of Dr. Soepraoen Malang Hospital. The hypothesis test used was Kruskal-Wallis. **Result:** The Kruskal-Wallis test found a significant association ($p = 0.046$; $p < 0,05$) between the time of first ASM administration and seizure control and a significant association ($p = 0.03$; $p < 0,05$) between the number of seizures before the first ASM administration and epileptic seizures. **Conclusion:** There are relationship between the time and number of seizures before the first ASM administration with controlled seizures.

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1. INTRODUCTION

Epilepsy is a progressive disease that is diagnosed after the occurrence of 2 or more unprovoked epileptic seizures [1]. The primary therapy for epilepsy involves the use of anti-seizure medication (ASM), which targets at least one specific mechanism [2], [3]. The treatment using ASM is considered effective when it demonstrates a seizure-free period of 12 months. This point is used to determine the efficacy of a particular ASM [4].

Not all epilepsy patients receive immediate treatment. Half of all epilepsy cases overall show a history of previously undiagnosed epileptic seizures [5]. Several factors influence the delay in patient treatment, such as the seizure type and socio-economic status [6]. (Parviainen, Kälviäinen and Jutila, 2020). The length of treatment gap increases the likelihood of more seizures occurring, thereby raising the possibility of epilepsy focus expansion [2].

Epilepsy focus expansion, also known as kindling, leads to a decreased sensitivity of the brain to treatment, resulting in Drug Resistant Epilepsy (DRE). DRE is a condition in which epilepsy in patients is considered resistant or unresponsive to treatment. One of the factors that can contribute to DRE is the occurrence of multiple epileptic seizures before initiating therapy [7].

2. METHOD

This study is an analytical observational quantitative research that collects secondary data to determine the relationship between the onset of anti-seizure medication (ASM) administration and seizure control in epilepsy patients at Dr. Soepraoen Level II Hospital in 2019 using a retrospective approach.

The data was obtained from medical records of patients diagnosed with epilepsy and meeting the inclusion criteria at the Neurology Outpatient Clinic of Dr. Soepraoen Level II Hospital in Malang from January to December 2019. The data analysis was performed using bivariate analysis between variables using statistical analysis such as chi-square. Since the chi-square requirements were not met, the Kruskal-Wallis test was used as an alternative. The sampling was conducted in December 2022 to January 2023 at the Neurology Outpatient Clinic of Dr. Soepraoen Army Hospital Hospital in Malang.

3. RESULTS AND DISCUSSION

The data was obtained from medical records of patients diagnosed with epilepsy and meeting the inclusion criteria at the Neurology Outpatient Clinic of Dr. Soepraoen Level II Hospital in Malang from January to December 2019. A total of 41 samples that met the criteria were obtained. In Table 1, the mapping of patient outcomes with a delay time of less than 6 months showed 12 samples, with 8 (19.5%) of them reported as controlled epileptic seizures and 4 (29.2%) as uncontrolled seizures, with the shortest interval being less than 1

Tabel 1 Distribusi Sampel Penelitian terhadap Terkontrolnya Bangkitan Epileptik

		Jumlah pasien dengan Bangkitan Epileptik terkontrol (%)	Jumlah pasien dengan Bangkitan Epileptik tidak terkontrol (%)	Total (%)
Keterlambaan Pengobatan	< 6 bulan	8 (19,5%)	4 (9,7%)	12 (29,2%)
	6 – 12 bulan	6 (14,6%)	6 (14,6%)	12 (29,2%)
	12 – 24 bulan	0 (0%)	5 (12,1%)	5 (12,1%)
	> 24 bulan	4 (9,7%)	8 (19,5%)	12 (29,2%)
Total		20 (48,7%)	22 (53,6%)	41 (100%)
Banyaknya Bangkitan	< 3	10 (24,3%)	7 (17%)	17 (41,4%)
	3 – 10	7 (17%)	8 (19,5%)	15 (36,5%)
	11 – 20	1 (2,4%)	5 (12,1%)	6 (14,6%)
	21 – 50	0 (0%)	3 (7,3%)	3 (7,3%)
Total		18 (43,9%)	23 (56%)	41 (100%)

day, indicating controlled seizures. Among the patients with a delay interval of more than 24 months, there were 12 samples, with 4 (9.7%) of them experiencing controlled epileptic seizures, while the remaining 8 (29.2%) had uncontrolled seizures. The longest interval reached more than 10 years, yet the patients' seizures were controlled.

From the data, it can be observed that approximately 30% of the samples experienced a delay in diagnosis of more than 2 years from the initial time point when patients should have been diagnosed with epilepsy, which is promptly after experiencing 2 unprovoked seizures or the first unprovoked seizure with a history of brain injury. In the patient mapping, a total of 17 samples were found to have less than 3 seizures. Among these, 10 (24.3%) samples had controlled epileptic seizures, while 7 (17%) samples had uncontrolled seizures. The lowest number of seizures observed was 1, preceded by a condition such as a previous stroke, with controlled seizure outcomes. There were 3 samples with seizure frequencies ranging from 21 to 50 seizures, with 0 (0%) samples having controlled seizures and 3 (7.3%) samples having uncontrolled seizures. The highest number of seizures recorded was over 40 seizures, with the final outcome being uncontrolled seizures. Most of the patients who experienced less than 10 seizures before starting ASM treatment had controlled seizures. On the other hand, the majority of patients with more than 10 seizures before receiving ASM treatment had uncontrolled seizures.

In the analysis of the relationship, the obtained p-value is 0.046, where $P < 0.05$. Therefore, it can be concluded that there is a relationship between treatment delay and the control of epileptic seizures in epilepsy patients at Dr. Soepraoen Level II Hospital in 2019. In the analysis of the relationship between the number of seizures and seizure control, the obtained p-value is 0.03, where $P < 0.05$. Hence, it can be concluded that there is a relationship between the number of seizures before ASM administration and seizure control in patients with epilepsy at Dr. Soepraoen Level II Hospital in 2019.

3.1. Hubungan Keterlambatan Pengobatan ASM dengan Terkontrolnya Bangkitan Epileptik

This study indicates that the longer the treatment delay interval from the second spontaneous seizure or the first spontaneous seizure preceded by a brain injury, the greater the impact on the final treatment prognosis, namely the control of epileptic seizures. Previous research stated that there is no direct relationship between the length of delay in diagnosis and the final treatment prognosis of epilepsy. However, it is the number of epileptic seizures that occur within that delay period that affects the final outcome of the treatment provided [6]. This is because within the same treatment delay period, different patients can experience varying numbers of seizures. It is this individual variation in the number of seizures that will affect the final treatment prognosis for each patient [8].

There are many factors that contribute to treatment delay, and one of them is the lack of frequent epileptic seizures occurring within the delay period, or the epileptic seizures that occur do not have a significant impact on the patient's daily life. As a result, patients may decide to postpone treatment [9]. Furthermore, the type of epileptic seizures also influences the treatment decisions of patients. Patients with focal onset epileptic seizures are more likely to experience treatment delays. This can occur because these types of seizures are often non-convulsive and can manifest as absence seizures, making them more difficult to identify [10].

3.2. Hubungan Banyaknya Bangkitan Epileptik Sebelum Pengobatan dengan Terkontrolnya Bangkitan

Furthermore, the type of epileptic seizures also influences the treatment decisions of patients. Patients with focal onset epileptic seizures are more likely to experience treatment delays. This can occur because these types of seizures are often non-convulsive and can manifest as absence seizures, making them more difficult to identify. One study that supports this statement is a study where researchers sampled epilepsy patients with focal seizures and assessed the relationship between the number of epileptic seizures before the diagnosis was established and seizure control in patients [6]. The study showed a significant relationship between the number of epileptic seizures and seizure control, indicating that the higher the number of seizures, the less likely they were to be controlled.

Brain damage or the occurrence of the first epileptic seizure occurs as a manifestation of a decrease in action potential threshold or the presence of hyperexcitability, leading to the brain adapting as a form of response through neuroplasticity. This process results in progressive changes at the cellular level, which extend to a reorganization of the nervous system. These changes are characterized by a latent phase between the occurrence of brain injury or the first seizure event and the onset of the second seizure without any provocation [11]. However, the changes that occur during epileptogenesis are not fully understood, leading previous researchers to develop the kindling model theory [12].

Kindling is an experimental procedure in which laboratory animals are repeatedly stimulated in a specific area of the brain until it eventually triggers a spontaneous epileptic seizure response [13]. This stimulation lowers the seizure threshold in the model and the presence of learning mechanisms in the brain, interpreted as memory, allows seizures to occur spontaneously [12]. The ability of brain neuroplasticity also influences the increased excitability of neurons, changes in synaptic connections, and modifications of neural tissue both structurally and functionally [13]. The areas of the brain that undergo structural and functional changes are referred to as epileptic foci, which lead to the occurrence of spontaneous epileptic seizures. These epileptic foci can expand, explaining how the generalization of epileptic seizures can occur [14].

3.3. Limitasi penelitian

This study has several limitations, one of which is its reliance on patients or caregivers to recall the number and type of epileptic seizures, which may introduce bias. Additionally, factors that may influence seizure control, such as patient compliance with treatment, cannot be systematically identified.

4. CONCLUSION

There is relationship between delayed therapy and controlled seizures in patients with epilepsy at Dr. Soepraoen army hospital 2019

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